Effects of a Multidisciplinary Intervention on the Presence of Neuropsychiatric Symptoms and Psychotropic Drug Use in Nursing Home Residents WithYoung-Onset Dementia

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Effects of a multidisciplinary intervention on the presence of neuropsychiatric symptoms and psychotropic drug use in nursing home residents with young-onset dementia: Behavior and Evolution of Young ONset Dementia part 2 (BEYOND-II) study

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Abstract

Objectives: The effect of an intervention on the presence of neuropsychiatric symptoms (NPS), particularly agitation and aggression, and psychotropic drug use (PDU) in institutionalized people with young-onset dementia (YOD) was evaluated.

Design: A randomized controlled trial was conducted using a stepped wedge design. Thirteen YOD special care units were randomly assigned to three groups, which received the intervention at different time points. Four assessments took place every six months during a period of eighteen months.

Setting and participants: Two hundred and seventy-four people with YOD residing on YOD special care units participated, of whom 131 in all assessments.

Intervention: The intervention consisted of an educational program combined with a care program, which structured the multidisciplinary process of managing NPS. The care program included the following five steps: the evaluation of psychotropic drug prescription, detection, analysis, treatment and evaluation of treatment of NPS.

Measurements: The Cohen-Mansfield Agitation Inventory and the Neuropsychiatric Inventory, nursing home version were used to assess NPS. Data on PDU was retrieved from residents' medical files. Multilevel models were used to evaluate the effect of the intervention, which accounted for clustering of measurements within clients, within units.

Results: No significant differences on agitation and aggression, other NPS, and PDU after crossing over to the intervention condition were found.

Conclusions: We found no evidence that the intervention for the management of NPS in nursing home residents with YOD was more effective in reducing agitation and aggression, other NPS, or PDU compared to care as usual.

Objective

When dementia occurs before the age of 65, this is most commonly referred to as young-onset dementia (YOD). Of the nursing home (NH) residents with YOD, 90% show one or more neuropsychiatric symptoms (NPS) (1). These high rates are troublesome given the serious negative health outcomes associated with NPS in dementia, such as loss of quality of life of the NH resident, high workload and distress of professional care givers, and increased costs of care (2-7). Comorbidity is less common at least in people in with young-onset Alzheimer disease than in people with late-onset Alzheimer disease, suggesting that people with YOD are less frail (8). As a consequence, NPS in YOD might be more severe compared to late-onset dementia (LOD) because of increased physical fitness, such as walking speed and strength. Indeed, a recent study by van Duinen-van den IJssel et al. (2017) showed that NH staff caring for people with YOD experience more distress related to NPS compared to NH caring for people with LOD (7). Psychotropic drug use (PDU) is common in the management of NPS in NH residents with LOD and YOD (9, 10). PDU is associated with poor health outcomes, such as stroke, increased mortality, and reduced quality of life (3, 11, 12). However, still between 76.9 - 87.6% of the NH residents with YOD use one or more psychotropic drug(s) (4, 9). Those rates seem higher compared to PDU in NH residents with LOD (9).

The high prevalence rates of NPS and PDU stress the need for the development and evaluation of nonpharmacological interventions in YOD. To successfully manage NPS, many models emphasize that the underlying causes of NPS need to be identified and treated (13). One of these models is the unmet-needs framework, in which NPS are perceived as behaviors through which the person with dementia might indirectly communicate an underlying need (13). Needs can be medical (e.g., physical illness, pain, and mobility), psychosocial (e.g., life habits, and premorbid personality), or environmental (e.g. under/over stimulation, and

behavior of NH staff/ other residents) (14, 15). People with YOD have specific age-related care needs regarding daytime activities, social interaction, intimate relationships, and information, which are often unmet (16). With knowledge of the underlying causes of NPS, an intervention can be individualized to the specific needs of the residents, instead of suppressing the behavior with the use of psychotropic drugs, concealing behavior through which the person with dementia might indirectly communicate an underlying need (14, 17, 18).

In the current study, the effect of a multidisciplinary intervention for the management of NPS in NH residents with YOD was evaluated (19, 20). The intervention was based on the "Grip on challenging behavior" care program that has shown effectiveness in the management of NPS in LOD (19-22).

The aims of the study are to (1) evaluate the effect of the intervention on the prevalence of NPS, particularly agitation and aggression, compared to care as usual, and (2) evaluate the effect of the intervention on PDU.

Methods

This cluster randomized controlled trial (RCT) is part of the Behavior and Evolution of Young-ONset Dementia, part 2 (Beyond-II) study (23). Process data was assessed in order to be able to interpret the outcomes of this RCT (24). The process data showed sufficient internal and external validity allowing for further effect analyses (24, 25).

Setting and subjects

In this study, thirteen YOD special care units (SCUs) participated, which are care units delivering specialized treatment and support for people with YOD (24). The YOD-SCUs were recruited through NHs that are affiliated with the Dutch YOD Knowledge Center (DKC).

Residents with a dementia diagnosis with a symptom onset before the age of 65 who resided on the YOD SCU for at least one month were eligible for inclusion in the study. The exclusion criteria were lack of informed consent provided by the legal representative, dementia caused by human immunodeficiency virus (HIV), traumatic brain injury, Down's syndrome, Korsakov syndrome or Huntington's disease. Diagnoses of dementia subtype were made before inclusion, according to internationally accepted criteria for diagnosing dementia subtypes and were retrieved from medical files (26-31). Newly admitted residents were recruited until the end of the study, replacing deceased residents and residents who moved to another care unit during the study.

Intervention

The development of the intervention 'Grip on NPS in institutionalized people with YOD' is described in detail elsewhere (20). To increase implementation, the NH staff received an educational program that consisted of 2 training sessions (of 2.5 and 1.5 hours). In the educational program, causes and mechanisms of NPS were discussed with the NH staff and the use and relevance of the care program was explained. After receiving the educational program, the care program on the management of NPS was implemented (figure 1). The care program provided guidance for the multidisciplinary team involved in the management of NPS in Dutch NHs to structure the process of detection, analysis, treatment, and evaluation of NPS. This care program consisted of five steps, which were consecutive and formed a cycle, except for the evaluation of appropriateness of psychotropic drug prescription. This separate step was a tool for the evaluation of appropriateness of psychotropic drug prescription by the elderly care physician (32, 33). The tool was performed for all residents (with or without NPS) in the first two months after the SCU was enrolled in the intervention condition. After the initial screening, the tool was used at the physician's own discretion. The other four

consecutive steps of the care program had a circular structure (figure 1). Detection of NPS occurred through usual observations of the multidisciplinary team or with the systematic use of a screening tool every six months by a vocational nurse. When NPS were detected, a structured analysis of possible causes of the NPS observed was conducted by the (vocational) nurse. This analysis included a tool for the detection of unmet needs possibly underling the NPS (34). When necessary, the elderly care physician and/or the psychologist continued the analysis. After this analysis, treatment options were discussed within the multidisciplinary team and a treatment plan was established by the elderly care physician and/or the psychologist. The care program did not prescribe a specific intervention. The choice of the intervention relied on the hypothesized causes of the NPS, the preferences of the resident, and the available options in the NH. However, psychosocial treatments were preferred, with PDU only if other treatments had little or no effect. The treatment outcomes were evaluated by the multidisciplinary team and if unsatisfactory, other treatments were considered or the analysis was performed again. All tools of the care program were fully digitalized and contained automatic reminders.

Design

To evaluate the effect of the intervention, a stepped wedge design was used (Table 1). This design allowed the YOD SCUs to crossover from the control to the intervention condition over time, assuring that all YOD SCUs received the intervention (35). The thirteen YOD SCUs were randomly assigned to three groups. Every six months a new group entered the intervention condition. The control condition consisted of care as usual without the educational program and use of the care program. Four assessments took place every six months during a period of eighteen months (September 2015 - April 2017).

Data collection and ethical considerations

The Beyond-II study protocol was approved by the Medical Ethics Committee region Arnhem/Nijmegen (file number 2015-1558) and registered in the Dutch Trial Register (Trial ID NTR5018). This research project was conducted according to the principles of the Declaration of Helsinki (version November 2013, www.wma.net) and in agreement with the laws regarding medical-scientific research in humans (WMO).

Written informed consent was obtained from the legal representative of each resident. After receiving informed consent, trained researchers and research assistants collected the data from the resident's medical files and through structured interviews with nursing staff.

Primary outcome

The Dutch version of the Cohen-Mansfield Agitation Inventory (CMAI-D) was used to assess *agitation and aggression* (14, 36). The CMAI has a well-established validity and reliability and assesses 29 agitated or aggressive behaviors (36). The frequency of each symptom is rated on a seven-point frequency scale (range 1-7) ranging from never to several times an hour. We used CMAI factors based on a previous study in LOD in which three CMAI factors in a large NH sample were found: physically non-aggressive behaviors (range 7-49), physically aggressive behaviors (range 8-56), and verbally agitated behaviors (range 4-28) (37).

Secondary outcomes

To determine effects of the care program on *other NPS*, the Dutch version of the Neuropsychiatric Inventory-nursing home version (NPI-NH) was used. The NPI-NH has a high interrater reliability and is found to be a valid instrument for the assessment of a wide range of NPS in dementia (38). The NPI-NH consists of twelve neuropsychiatric symptoms:

delusions, hallucinations, agitation/aggression, depression, anxiety, euphoria, apathy, disinhibition, irritability, aberrant motor, nighttime behavior disturbances, and eating disturbances. For each symptom a screening question is used to determine whether the symptom is present. If the symptom is present, Frequency (F) and Severity (S) are rated on a four-point (ranging from 1-4) and three-point Likert-scale (ranging from 1-3), for each symptom, respectively. Scores for each symptom are calculated as F x S (ranging from 1-12). A symptom score of at least 4 is considered clinically relevant (39).

PDU was derived from the nursing homes pharmacists' electronic files and was classified according to the Anatomical Therapeutic Chemical (ATC) classification system into antipsychotics, anxiolytics, hypnotics, antidepressants, anti-epileptics, anti-dementia drugs, and any psychotropic medication (40). Medication as needed, which is medication that is not taken according to a fixed schedule but only given in the prescribed dosage if needed, was not included because it was unclear if and how often these drugs were actually used. Furthermore, anti-epileptics used by residents with epilepsy were not registered as PDU.

Other measurements

Medical and demographic data were extracted from the resident's medical files. Data on dementia subtype, age, gender, length of stay at the SCU, and date of inclusion were recorded. *Dementia severity* was assessed with the Global Deterioration rating Scale (GDS) (41). The GDS describes seven different stages of dementia on a seven-point scale (1-7), ranging from "subjectively and objectively normal cognition" to "severe cognitive decline".

Process data showed that the fidelity of the intervention differed between SCUs (24). Therefore, fidelity was conceptualized into an implementation score consisting of three components. A score was calculated for the step detection based on the number of times the step was completed with regard to the number of residents residing on the SCU (score 2 if

used at least once every six months for 75-100% of all residents, score 1 if used for 50-74%, score 0 if used in <50%) (24). In addition, the NH staff rated the percentages of cases with challenging behavior in which they worked according to the care program on a questionnaire (score 2 if used in 75-100% of the cases, score 1 if used in 50-74%, score 0 if used in <50%). At last, two authors closely involved in the implementation (J. D. and B. A.) separately rated the implementation based on their communication with the SCUs about the progress of the implementation (ranging from 0-2). Disagreements were solved by discussion. The scores on the three components were summed, resulting in a total implementation score (ranging from 0 – 6).

Statistical analysis

All analyses were performed using the Statistical Package for the Social Sciences (SPSS) version 22. Demographic variables of the NH residents at time of enrolment in the study were described by means or proportions.

Multilevel model analyses were used to adjust for the clustering of residents in the thirteen different SCUs (random effect for SCU) and the correlation of the repeated measures within the residents (random effect for resident, nested within SCU). Time and interaction of time with treatment were included as a fixed effect to model time trend (in absence of treatment) and the effect of treatment, respectively. Multilevel models were fitted with the restricted maximum likelihood method and the 95%-confidence intervals and p-value of the coefficients in the model were based on Wald-test and t-distribution with Satterthwaite approximation of the degrees of freedom. The twelve symptom scores on the NPI-NH were dichotomized into clinically relevant symptoms (symptom score ≥4) or no clinically relevant symptoms (symptom score <4). Data on PDU was also dichotomized (present or absent) for each category. In case of binary variables, the fit for logistic and linear mixed model logistic

regression were compared by comparing the observed and predicted profiles of SCUs over time. In the case of an equal or better fit, we used linear regression instead of logistic regression as this allows a direct interpretation in terms of change of percentage over time.

In a previous study evaluating the effect of the intervention in LOD, dementia severity and time being exposed to the intervention had an influence on the intervention effect (21). In addition, differences in fidelity between SCUs could influence the intervention effect (24). Therefore, to investigate whether the intervention effect was different for residents with more advanced dementia (GDS score <5 mild, score = 5 moderate, or score ≥6 severe), or for residents exposed to the intervention for a longer period of time (0-6 months, 6-12 months, or 12-18 months), or for a higher fidelity (implementation score), interaction effects between the intervention and these variables were investigated. In all analyses, a *p* value <0.05 was considered statistically significant.

Results

In total, 274 NH residents with YOD participated in this study. Table 2 provides demographic and clinical characteristics of the nursing home residents at time of inclusion. Seventy-six residents were lost to follow-up because they moved to another care unit or deceased before the end of the study. Sixty-seven newly admitted residents were included after T0.

For all variables (including binary variables), linear multilevel regression models were used because these models had a better or equally good fit, and in case of binary variables, were consistent with the logistic multilevel models in terms of the predicted percentage in each of the institutions at each of the time points or better. In face of this consistency, we have chosen for the linear mixed model as this has an easier interpretation as absolute difference in percentages. The analyses showed no significant effect of the intervention on physically aggressive behaviors (Estimate=.495, p=.303), physically non-aggressive behaviors

(Estimate=-.137,p=.825), and verbally agitated behaviors (Estimate=-.176, p=697) (Table 4.). Additionally, no effect of the intervention on other NPS and PDU was found (Table 4.).

No significant interaction effects between dementia severity and fidelity and the intervention effect were found. A significant interaction effect for the effect of the intervention and the time that a resident was exposed to the intervention with regard to the prevalence of delusions was found (p = .024). After being exposed for a longer period of time to the intervention it became more effective in decreasing delusions, with an estimated intervention effect of -.06 (p = .056) for SCUs which worked 0-6 months with the intervention to an estimated intervention effect of -.06+2*-.06 (estimated intervention effect = -.18, p =0.08) for SCUs working 12-18 months with the intervention.

Discussion

To our knowledge, this is the first study that evaluated the effects of a multidisciplinary intervention on the management of NPS in NH residents with YOD on the presence of NPS, particularly agitation and aggression, and PDU. We found no evidence that the intervention was more effective in reducing agitation and aggression, other NPS, or PDU compared to care as usual.

An intervention for the management of NPS and PDU in LOD, on which our intervention was based, was able to diminish NPS and PDU (21). An explanation for the differences in effects between the original intervention and the adapted intervention for YOD might be that all participating SCUs in our study were recruited through NHs that were affiliated with the DKC. Only care organizations offering specialized care for people with YOD are affiliated with the center. Therefore, they might have already (to some degree)

developed effective working methods for the management of NPS in YOD before implementation of our intervention. Indeed, the process evaluation revealed that the NH staff experienced overlap between the intervention and their current working methods (24). In addition, although most NH staff was satisfied with the overall content of the care program, some steps of the intervention (like detection and tool to monitor PDU) were often rated as irrelevant (24). This suggests that users of the intervention did not expect that these steps would be more effective in diminishing NPS and PDU compared to care as usual in YOD SCUs. Possibly, in YOD SCUs there was less need for an intervention, which structured the management of NPS compared to LOD care units. The needs from one setting (LOD care units) cannot be completely generalized to another setting (YOD SCUs).

Despite adding a tool to the intervention for monitoring PDU, no significant decrease in PDU after implementation of the intervention was found. A possible explanation could be that the current policy that favors limiting the prescription of psychotropic drugs, has already positively influenced the prescription pattern to some degree, leaving less room for improvement. Indeed, when comparing the PDU rates in our study (68.6% using at least one drug) with the PDU rates in NH residents with YOD approximately 10 years ago (87.6% using at least one drug), the PDU rates in our study appear considerably lower (4).

Our results suggest that after working longer with the intervention, it became more effective in decreasing delusions. However, not even a trend towards increasing or decreasing effectiveness was found for other NPS. Therefore, we expected that this interaction effect might have been a result of multiple testing.

An important strength of this study was that we were able to include a large sample size of NH residents, resulting in sufficient study power (80% for an effect of 0.4xSD) (23). This is an advantage, especially in research on YOD, because the prevalence of NH residents with YOD is much lower compared to LOD. Also, some limitations of this study should be

considered. The presence of NPS was based on observations of nurses who could not be blinded. Awareness of being in the intervention or control condition might have influenced their ratings to some degree. Furthermore, no assessment instruments are available which take into account the specific characteristics of younger individuals with dementia. Therefore, we chose to measure NPS with assessment instruments designed and validated for the use in NH residents with LOD (36, 38). However, the CMAI does not extensively assess behavior associated with frontal lobe dysfunction, which might be more likely to occur in younger NH residents with dementia because of the higher prevalence of FTD (1). At last, we decided to not include medication as needed in the effect analysis, because in our study we did not collect data on how often these drugs were actually used. Therefore, we could not establish the influence of the intervention on the admission of medication as needed.

Conclusions

We found no evidence that the intervention was more effective in reducing agitation and aggression, other NPS, or PDU compared to care as usual. The perceived overlap between the intervention and their current working methods and the lower PDU rates compared to approximately 10 years ago, suggests that YOD SCUs have already (to some degree) developed effective working methods for structuring the management of NPS in YOD before implementation of our intervention, diminishing the intervention effect. In future studies, more research on the specific needs and context of YOD SCUs during the development phase of an intervention is important to improve relevance and effectiveness of an intervention in this specific context.

Disclosure Statement

All authors declare no conflicts of interest.

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Tables and Figures

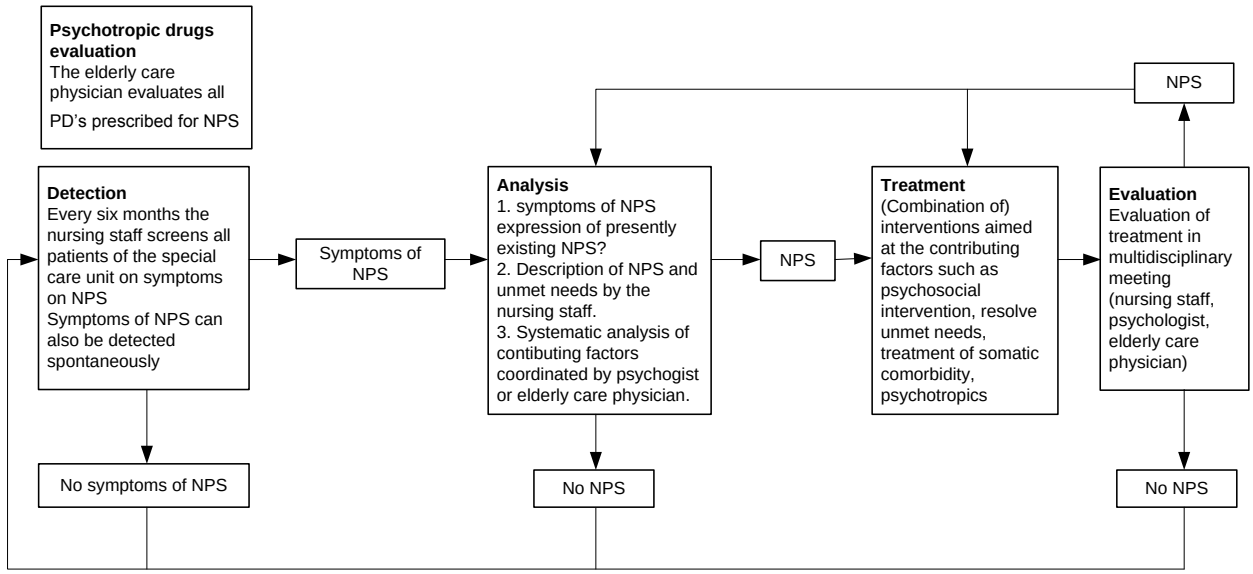

Figure 1. The five steps of the care program 'Grip on NPS in institutionalized people with YOD (23).

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NPS = Neuropsychiatric Symptoms, PD's = Psychotropic Drugs.

Table 1. Stepped wedge design

	Group 1	Group 2	Group 3‡
T0	0 *	0	0
T1	1 †	0	0
T2	1	1	0
T3	1	1	1

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* 0 = control condition

†1= intervention condition.

There are four, half yearly assessments. Each group consists of four or five YOD-SCU'S

Table 2. Demographic and clinical characteristics of the nursing home residents at time of inclusion (n = 274)

Age	Mean (SD *)	63.86 (5.91)
	[Range]	[39-78]
Gender	Male n (%)	138 (50.4)
Length of stay at the SCU† (months) ‡	Mean (SD)	28.65 (32.10)
	[Range]	[1-259]
Dementia severity (GDS§)||	n (%)	
Mild (2,3,4)		43 (15.7)
Moderate (5)		57 (20.8)
Severe (6,7)		172 (62.8)
Dementia subtype	n (%)	
Alzheimer' disease		120 (43.8)
Vascular dementia		29 (10.6)
Frontotemporal dementia		80 (29.2)
Mixed Alzheimer/vascular		14 (5.1)
Lewy Body/ Parkinson		5 (1.8)
Alcohol related dementia		6 (2.2)
Other		20 (7.3)

* SD = Standard Deviation
† SCU = Special Care Unit
‡ = 1 missing
§ GDS = Global Deterioration Scale
|| = 5 missing

Table 3. Baseline data on outcome variables at the time of inclusion (n=227)*

CMAI† factor scores	Mean (SD‡)	
Physically aggressive behaviors		13.02 (6.41)
Physically nonaggressive behaviors		14.86 (7.90)
Verbally agitated behaviors		8.46 (5.90)
Clinical relevant NPI-NH§	n (%) with Mean FxS|| (SD)	
Delusions		29 (12.8) 8.45 (2.87)
Hallucinations		29 (12.8) 6.86 (3.01)
Agitation/Aggression		95 (41.9) 7.27 (2.80)
Depression		42 (18.5) 7.29 (3.08)
Anxiety		33 (14.5) 8.18 (3.02)
Euphoria		23 (10.1) 8.04 (3.14)
Apathy		93 (41.0) 8.52 (3.28)
Disinhibition		69 (30.4) 8.07 (3.00)
Irritability		84 (37.0) 7.63 (2.63)
Aberrant motor behavior		89 (39.2) 8.47 (3.30)
Nighttime behavior disturbances		37 (16.3) 7.57 (2.97)
Eating disturbances		43 (18.9) 7.56 (2.86)
PDU**	n (%)	
Antipsychotics		71 (31.3)
Anxiolytics		60 (26.4)
Hypnotics		34 (15.0)
Antidepressants		80 (35.2)
Anti-epileptics		22 (9.7)
Anti-dementia drugs		12 (5.3)
Any psychotropic medication		152 (67.0)

* Only the scores for residents included at T0 and residents included at T1 or T2 which not yet had been exposed to the intervention are shown.

† CMAI = Cohen-Mansfield Agitation Inventory

‡ SD = Standard Deviation

§ NPI-NH = Neuropsychiatric Inventory-nursing home version

|| Mean F x S = mean frequency x severity scores of clinical relevant NPI-NH scores

**PDU = psychotropic drug use

Table 4. Effects of the intervention on NPS and PDU

	Estimate	P	95% CI	
			Lower bound	Upper bound
CMAI factor scores*				
Physically non-aggressive behaviors	-.137	.825	-1.358	1.074
Physically aggressive behaviors	.495	.303	-.448	1.438
Verbally agitated behaviors	-.176	.697	-1.065	.713
Clinical relevant NPI-NH†				
Delusions	-.048	.136	-.111	.015
Hallucinations	.044	.135	-.014	.101
Agitation/aggression	-.001	.975	-.090	.087
Depression	.022	.560	-.052	.096
Anxiety	.034	.318	-.033	.102
Euphoria	.031	.338	-.033	.095
Apathy	.051	.320	-.051	.154
Disinhibition	.077	.092	-.013	.167
Irritability-	.000	.999	-.087	.087
Aberrant motor behavior	.049	.284	-.041	.139
Nighttime behavior disturbances	.050	.180	-.023	.122
Eating disturbances	.044	.253	-.031	.118
PDU‡				
Antipsychotics	-.002	.956	-.064	.060
Anxiolytics	-.033	.301	-.095	.029
Hypnotics	-.021	.459	-.078	.035
Antidepressants	-.057	.066	-.117	.004
Anti-epileptics	.029	.126	-.008	.067
Anti-dementia drugs	-.005	.781	-.045	.044
Any psychotropic medication	-.023	.505	-.090	.044

Estimate (i.e. regression coefficient) from multilevel model analyses with random effect for SCU and a random effect for resident, nested within SCU. P-value and 95%-CI were based on Wald-test and t-distribution with Satterthwaite approximation for the degrees of freedom.

* CMAI = Cohen-Mansfield Agitation Inventory

† NPI-NH = Neuropsychiatric Inventory-nursing home version

‡ PDU = psychotropic drug use